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10/030,605	05/31/2002	Ulrike Fiedler	1406/37	8368

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EXAMINER

BORIN, MICHAEL L

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 04/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

10/030,605

**Applicant(s)**

FIEDLER ET AL.

**Examiner**

Michael Borin

**Art Unit**

1631

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 10 January 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,3-12,14-18 and 20-46 is/are pending in the application.
- 4a) Of the above claim(s) 17-25,29-41 and 43-45 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-11,16,26-28,42,46 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Status of Claims***

1. Amendment filed 1/10/2006 is acknowledged. Claims 2,13,19 are canceled. Claim 46 is added. Claims 1,3-12,14-18,20-46 are pending. Claims 17, 18-25,29-41,43-45 remain withdrawn from consideration. Claims 14, 15 previously addressed as withdrawn from consideration is now included in the rejection of record.

2. Applicant's arguments have been fully considered and they are deemed to be persuasive-in-part. Rejections made under 35 USC 112, first paragraph (written description ), and 35 USC 102 are withdrawn in view of amendments to the claims. Rejection under 35 USC 112, first paragraph (scope of enablement) is modified in view of amendments to the claims.

### ***Sequence Listing***

3. Objection to specification addressing lack of SEQ ID Nos is withdrawn in view of amendments to specification. Claim 15 which appears to be directed to gamma-II-crystalline mutants is included in the consideration.

### ***Claim Rejections - 35 USC § 112, first paragraph.***

4. Claims 1,3-11,16,26-28,42,46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for mutants of bovine gamma crystallin

of SEQ ID No. 22 obtained by mutations at positions identified in claim 12, does not reasonably provide enablement for mutants of other crystallins, much less for other proteins with mutations at beta sheet structure as claimed.

Specification teaches that the initial protein, gamma-II-crystalline “has no binding properties whatsoever” (p. 4, second paragraph). For this protein, eight amino acid positions were randomized by site-specific mutagenesis which resulted in 26 billion (!) protein sequences (p. 13, last paragraph). Out of those only one carries the “expected amino acid exchanges” (p. 13, third full paragraph).

The breadth of the claims encompasses any protein comprising beta sheet and mutated at any residue located in at least two beta strands of at least one beta sheet <sup>1</sup>. Except for gamma-II-crystalline described above, specification does not provide any working examples of any other mutants of crystallins mutated at any other residues than the residues indicated for SEQ ID No. 22. Nor there is any guidance on what residues are to be mutagenized in any other proteins.

The mutants of the invention, as now claimed, have functional limitation of having new or improved antigen binding specificity. Specification teaches, in general, that “after the mutagenesis the beta sheet protein thus possesses antibody-like properties” (p., 12, second paragraph). Except for binding to BSA estradiol achieved for mutants of bovine gamma crystallin of SEQ ID No. 19 and 21, no “new or improved antigen binding specificity” is described neither for any other proteins nor for any other

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<sup>1</sup> Note that specification does not confirm that the selected residues of gamma crystalline are indeed located in at least two beta strands of at least one beta sheet as required by the claims; the latter general statement requiring to modify residues located in at least two beta strands of at least one beta sheet (p. 12, bottom) addresses any protein in general.

antigens. There is no guidance in specification on what core structure is required for the claimed functional limitation.

It is well known in the art that it is difficult to predict the functional effects of random single amino acid substitutions, and nearly impossible to predict the functional effects of multiple amino acid substitutions. The relationship between the sequence of a peptide and its tertiary structure (and thus its binding activity) are not well understood and are not predictable (see Guo et al, for example)

In view of the above, it is the Examiners position that with the insufficient guidance and working examples and in view of unpredictability and the state of art one skilled in the art could not make and/or use the invention with the claimed breadth without an undue amount of experimentation.

#### Response to arguments

Applicant argues that specification informs of other proteins that can be "similarly mutagenized". The issue, however, is not a potential similarity in beta sheet structure of various proteins, but rather a lack of guidance (except for gamma crystalline of SEQ ID No. 22) for what elements of structure can be mutagenized to obtain mutants with the claimed functional activity. The fact that other proteins share such structural features as beta sheet or Greek key motif does not provide guidance on how to select residues now loosely defined as "located in at least two beta strands of at least one beta sheet" and how to mutagenize them (whether it should be a substitution, or deletion/ insertion of an

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unspecified number of residues) to arrive at a mutant with the claimed functional activity of having "new or improved binding specificity" to an unspecified antigen.

5. Claims 12,15 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

 Michael Borin, Ph.D.  
Primary Examiner  
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